rate rod using Nylon mesh and metal wire. The rod was then reciprocated in a fixed volume of receptor solution (distilled water) at 32°C.

[00082] At given time intervals, the entire receptor solution was removed from the test tubes and replaced with an equal volume of fresh receptor solutions previously equilibrated at 32°C. The nicotine concentration in the distilled water receptor was measured by UV absorption at 260 nm. From the drug concentration and the volume of the receptor solutions, the area of permeation and the time interval, the flux of the drug was calculated as follows: (drug concentration X volume of receptor)/(area x time) = flux ($\mu g/cm^2$ hr). The results are shown in Table 4.

TABLE 4
Nicotine Flux ($\mu g/cm^2$ hr) Through
Annealed and Non-Annealed HDPE Films

HDPE Resin	Film Treatment	Thickness (mil)	Nicotine Flux
LP 5102	Non-annealed	1.90	31.47
LP 5102	Annealed	1.90	44.13
LR 723	Non-annealed	2.40	20.67
LR 723	Annealed	2.40	26.19
LR 734	Non-annealed	2.13	11.41
LR 734	Annealed	2.13	15.15
LS 901	Non-annealed	1.23	19.09
LS 901	Annealed	1.23	22.78

[00083] As seen from Table 4, the systems comprising annealed membranes resulted in a greater flux of nicotine than systems comprising non-annealed rate controlling membranes.

EXAMPLE 6

[00084] The effect of the vinyl acetate content on the permeability of EVA rate controlling membranes using testosterone as the model drug was investigated. A reservoir gel comprising 26 wt.% testosterone, 1-2 wt.% hydroxypropyl cellulose, and the remainder 95% ethanol was prepared by

mixing testosterone, 95% ethanol and adding hydroxypropyl cellulose with mixing.

[00085] A contact adhesive composition was made by mixing polyisobutylene (MW 1,200,000), polyisobutylene (MW 35000) and light mineral oil. A 50 micron thick layer of the contact adhesive was cast onto a 75 micron thick film of siliconized polyethylene terephthalate peelable liner. The contact adhesive side of the resulting two layer subassembly was laminated to a 50 micron thick film of annealed or non-annealed ethylene vinyl acetate (EVA) copolymer of various vinyl acetate content as set forth in Table 5. The annealed EVA membranes were heated at 42 °C for 5 days. The gelled testosterone-ethanol mixture was placed on the EVA membrane. A backing member comprised of aluminized polyethylene terephthalate with an EVA heat sealable coating was laid over the gels and heat-sealed to the EVA copolymer using a rotary heat seal machine. Finished systems were die-cut from laminate using a circular punch and placed in sealed pouches to prevent loss of volatile components.

[00086] The peelable liner of the laminate was removed and the system was then mounted on a Teflon® rod. A known volume of receptor solution (0.10% phenol/H_2O) was then placed in a test tube and was equilibrated at 35°C. The Teflon rod with the attached system was then placed in a water bath at 35°C. Mixing was accomplished by attachment to a motor which caused constant vertical mixing.

[00087] At given time intervals, the entire receptor solution was removed from the test tubes and replaced with an equal volume of fresh receptor solutions previously equilibrated at 35°C. The receptor solutions were stored in capped vials at 4°C until assayed for testosterone content by HPLC analysis. From the drug concentration and the volume of the receptor solutions, the area of permeation and the time interval, the flux of the drug was calculated as follows: (drug concentration X volume of receptor)/(area x time) = flux ($\mu g/cm^2 \cdot hr$).

TABLE 5
Average Release Rate of Testosterone Through
Annealed and Non-Annealed EVA Membranes of Varying VA Content

% Vinyl Acetate (VA)	AVG (12-30 hr) Testosterone release rate through non-annealed membrane ($\mu g/cm^2 \cdot hr$)	AVG (12-30 hr) Testosterone release rate through annealed membrane ($\mu g/cm^2 \cdot hr$)
12.2	1.39	1.56
9	1.04	1.22
9	1.02	1.21
6.6	0.46	0.50

EXAMPLE 7

[00088] 10 cm^2 systems containing fentanyl were prepared as set forth in Example 1. EVA membranes (thickness of 50 micron) comprising 6.6% VA were compared to systems comprising 9 % VA. The systems were exposed to various thermal stresses prior to conducting *in vitro* release rate studies following the procedure set forth in Example 1 to determine if membrane permeability exceeded a preferred maximum limit after thermal stressing. The preferred maximum release from the system is less than 34.5 $\mu g/cm^2 \cdot hr$ for the period 0-2 hours after application, less than 6.8 $\mu g/cm^2 \cdot hr$ for the period 2-12 hours after application, and less than 4.7 $\mu g/cm^2$ hr for the period 12 - 24 hours after application. As seen in Table 6, the annealed EVA 9 membrane exceeded the predetermined limits for the 0-2 and 2-12 hr intervals while the annealed EVA 6.6 membrane was within these limits after thermal stressing at 50°C for one day.